Feed Restriction in Swiss CD-1 Mice

No CAS #
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In this study the effects of feed restriction (FR) and reduced body weight gain, on various reproductive end points was evaluated (Chapin et al., Fundam Appl Toxicol 20:15–22 [1993]). The intent was to mimic the situation when animals on study eat poorly and gain weight more slowly than controls. Swiss CD-1 mice were fed standard rodent chow at levels sufficient to maintain body weights of 90, 80, and 70% of ad libitum control body weight (CBW, see the introduction to the preceding mouse FR study).

After a 5-week reduction period, animals were maintained within 3% of their target weight by daily feeding and body weights. Blackening of the tail tip was the most common clinical sign, which varied with both duration and degree of FR. Each male was cohabited with two nonrestricted females during study weeks 8 and 15. At week 8, fewer of the 70% males sired two litters. Litters from all FR males had fewer pups (11, 14, 12% fewer, from least to most FR, respectively), though the viability and weight of those pups was the same across groups. During the second mating trial (at study week 15), males from all FR groups sired equal numbers of litters, the litters were the same size, and the viability and weight of the pups were equal across groups.

Estrous cyclicity was evaluated in FR females prior to FR, and during weeks 8 and 15 of FR. Cycle length was increased in the 80 and 70% CBW groups only at the 15-week time point, when approximately half the females in each group were acyclic.

Females were mated with unrestricted males during study week 17, maintained on the FR regimen, and allowed to deliver their litter. As might be expected, the number of live pups per litter was greatly reduced at 90 and 80% CBW; no live pups were delivered at 70% CBW. The proportion born alive was less than half the control, and adjusted pup weight was reduced by 40 and 26% (for 90 and 80% CBW groups, respectively). Live pups appeared structurally normal.

At necropsy, male body weights were 85, 77, and 69% of control values. Similar to the first study, absolute testis weight was reduced by 10 and 14% in the middle and high dose groups. Absolute weights of liver, kidney, seminal vesicles, and epididymis were reduced in all FR groups. Interestingly, relative weights were variably changed: liver weight was decreased approximately 15% in all FR groups, adjusted epididymis and kidney weights were unchanged, while adjusted cauda epididymis weight was increased approximately 15% in all FR groups. Epididymal sperm concentration was reduced by approximately 30% at 70% FR, but no other sperm indices were affected. Intriguingly, intratesticular testosterone (ng/g testis) was reduced by 60, 54, and 85% in the least, middle, and most restricted groups, respectively.

In females, killed after delivering their litters, body weights were reduced to 89, 69, and 69% of control values. Absolute weights of liver, kidney, and uterus were decreased in all dose groups. Relative liver weights decreased by 7, 12, and 18, while relative uterus weight was decreased by 30 and 50 in the middle and most restricted groups, respectively. Significant FR-related microscopic lesions were limited to hypoplasia of the ovary and uterus in the 70% CBW mice.

Thus, this study found longer estrous cycles at weeks 15 to 16 in the 80 and 70% CBW females, and reduced pup number and weight in all restricted females. Male fertility was variably affected; only sperm count reduced, and that only with the greatest FR.

Summary: NTP Reproductive Assessment by Continuous Breeding Study.

NTIS#: **92174259**
Chemical: **Feed Restriction**
CAS#: **NA**
Mode of exposure: **NA**
Species/strain: **Swiss CD-1 mice**

F_0 generation Restriction levels→	90% BWT	80% BWT	70% BWT
General toxicity	Male, female	Male, female	Male, female
Body weight	↓ , ↓	↓ , ↓	↓ , ↓
Kidney weight[a]	— , —	— , —	— , —
Liver weight[a]	↓ , ↓	↓ , ↓	↓ , ↓
Mortality	— , —	— , —	— , —
Clinical signs	↑ , ↑	↑ , ↑	↑ , ↑
Reproductive toxicity, male mating trial 1			
$\bar{x}$ litters/male	—	—	—
# live pups/litter; pup wt./litter	↓ , ↓	↓ , ↓	↓ , ↓
Reproductive toxicity, male mating trial 2			
$\bar{x}$ litters/male	—	—	—
# live pups/litter; pup wt./litter	— , —	— , —	— , —
Absolute testis, epididymis weight[a]	— , ↑	↓ , ↑	↓ , ↑
Sex accessory gland weight[a] (prostate, seminal vesicle)	— , —	— , ↓	↓ , ↓
Epidid, sperm parameters (#, motility, morphology)	— , — , —	— , — , —	↓ , — , —
Reproductive toxicity, female mating trials after 17 weeks feed restriction			
# live pups/litter; pup wt./litter	↓ , ↓	↓ , ↓	↓ , ND
Dam wt. at delivery	↓	↓	↓
Estrous cycle length, prior to diet restriction	—	—	—
Estrous cycle length, during diet restriction	—	—	—
Estrous cycle length, after diet restriction	—	↑	↑

Summary information	
Affected sex?	Both
Study confounders:	None

Legend: —, no change; •, no observation; ↑ or ↓, statistically significant change ($p<0.05$); — , —, no change in males or females; ND, no data. [a]Adjusted for body weight.